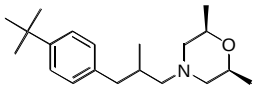
5.12 FENPROPIMORPH (188)

RESIDUE AND ANALYTICAL ASPECTS

Fenpropimorph is a systemic morpholine fungicide for the control of various diseases primarily in cereals but also finds use in controlling Sigatoka diseases in bananas. It acts by inhibiting the sterol pathway of fungus. The ADI for fenpropimorph was re-established as 0–0.004 mg/kg bw in 2016 and ARfDs of 0.1 mg/kg bw for women of child-bearing age and 0.4 mg/kg bw for the general population established. At the 47th Session of the CCPR (2015), it was scheduled for the evaluation of residues by 2017 JMPR under the periodic review program of CCPR.

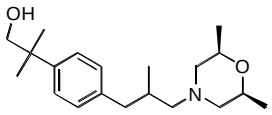
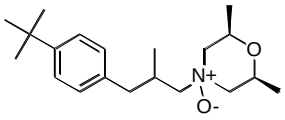
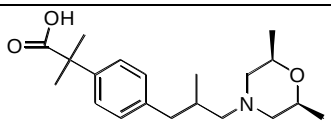
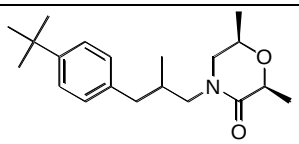
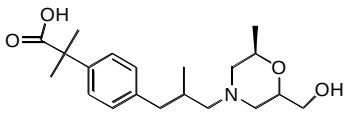
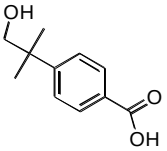
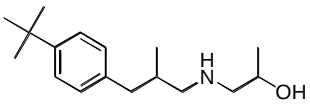
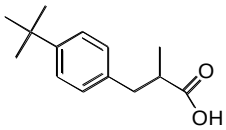
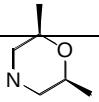
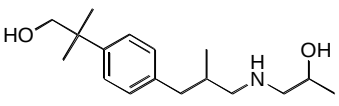
The Meeting received information on the metabolism of fenpropimorph in lactating goats and laying hens, banana, sugar beet, barley and wheat, follow crops, methods of residue analysis, freezer storage stability, GAP information, supervised residue trials on banana, sugar beet, barley, oats and wheat as well as a livestock feeding study (lactating cow).

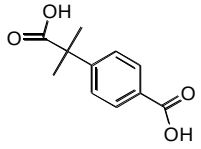
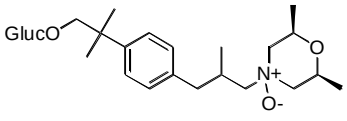
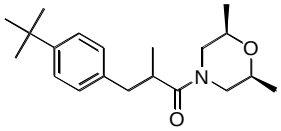
Fenpropimorph is (±)-*cis*-4-[3-(4-*tert*-butylphenyl)-2-methylpropyl]-2,6-dimethylmorpholine.



Fenpropimorph is a racemate, that is it consists of equal amounts of two enantiomers.

Metabolites referred to in the appraisal are addressed by their company codes:

Code	Structure	Code	Structure
BF421-1		BF421-14	
BF421-2		BF421-15	
BF421-3		BF421-16	
BF421-7		BF421-18	
BF421-10		BF421-20	

Code	Structure	Code	Structure
BF421-12		BF421-36	
BF421-13			

Studies on the metabolism in plants and livestock and environmental fate utilised [phenyl U-^{14}C]-fenpropimorph = P-label, [morpholine-2,(6)-^{14}C]-fenpropimorph = M1-label, [morpholine-2,6-^{14}C]-fenpropimorph =M2-label, and [benzylic-^{14}C]-fenpropimorph = B-label.

Plant metabolism

The Meeting received plant metabolism studies with fenpropimorph following foliar applications to banana, sugar beet, barley and wheat.

Banana

The metabolism of [^{14}C]-fenpropimorph, labelled in the morpholine (M2-label) or phenyl (P-label) rings, in banana plants was studied in plants grown outdoors following four foliar sprays at 0.9 kg ai/ha at intervals of 14, 51 and 12 days. The experiment included plants where bunches were protected (bagged) after the first spray and those where bunches remained unprotected (unbagged). Fruits are unripe at harvest and a sample of fruit was ripened using acetylene.

TRRs found in whole fruit at harvest (0 days after the last application) were higher in unbagged (0.09–0.67 mg eq/kg) compared to bagged bunches (0.025–0.35 mg eq/kg). TRR was also higher in experiments using the M2-label compared to the P-label.

In whole fruit, methanol extracted ^{14}C ranged from 27 to 83% TRR for the M2-label, whereas the corresponding values varied between 49 to 88% TRR for the P-label.

Fenpropimorph accounted for 3.2 to 16% of the TRR in whole fruit from the M2-label experiments, with sugars the only other major component identified (accounting for 9.7 to 76% TRR, the higher levels occurring in ripened fruit). For the P-label, fenpropimorph accounted for 14 to 60% of the TRR in whole fruit with no other component identified. Levels were too low to permit identification of ^{14}C in PES.

In summary, metabolism of ^{14}C-fenpropimorph in banana proceeds with hydroxylation of the *t*-butyl at the phenyl ring, followed by glucosidation. The morpholine ring can be degraded with its C_1 fragments utilised during assimilation processes in the plant for the biosynthesis of carbohydrates.

Sugar beet

Two studies were made available on the metabolism of ^{14}C-fenpropimorph in sugar beet.

In the first, two foliar applications of an EC formulation of ^{14}C-fenpropimorph labelled in the morpholine ring (M1-label) were made to sugar beet in a glasshouse at 0.15 kg ai/ha at BBCH 39 and at 32 days before harvest. TRRs were lower in roots (0.026 to 0.034 mg eq/kg) and the higher in leaves (0.596 to 1.885 mg eq/kg) demonstrating limited translocation from treated leaves into the roots.

Methanol extracted >70% of the ^{14}C in roots (70–79% TRR) and >79% from leaves (79–92% TRR).

In roots, other than natural products, the major component identified was fenpropimorph, comprising 40% TRR at 0 days and 14% TRR at 32 days after the second application. In leaves, fenpropimorph accounted for 14–15% TRR. Three metabolites were identified; BF421-1 glucoside (max 10% TRR), BF421-1 diglucoside (max 15% TRR) and BF421-1 glucoside sulphate (maximum 22% TRR). Glucose accounted for 34–56% TRR in roots and 4.3–9% TRR in leaves. A small amount of ^{14}C in leaves was associated with other natural products such as cellulose and lignins.

The second study utilised EC formulations of ^{14}C-fenpropimorph labelled in either the morpholine or phenyl rings. A single application was made to sugar beet maintained in a glasshouse at 0.75 kg ai/ha with harvest 112 days after treatment. The highest levels of TRRs were found in sugar beet plants sampled on the day of application (55.2 mg eq/kg P-label, 47.2 mg eq/kg M1-label). The TRR values for sugar beet leaves harvested 112 DALA amounted to 0.97 mg eq/kg for the P-label or 0.52 mg eq/kg for the M1-label. In sugar beet root, the ^{14}C levels were much lower, accounting for 0.03 mg eq/kg (P-label) to 0.04 mg eq/kg (M-label).

The extractability of ^{14}C with methanol was high for sugar beet leaves (89–93 %TRR) and quite good for sugar beet root (64–76 %TRR).

The major components identified in roots were fenpropimorph (17–34% TRR), BF421-20 glucoside (11% TRR), BF421-1 diglucoside (15% TRR) and sugars (23% TRR). In leaves the major components were fenpropimorph (5–19% TRR), BF421-14 (7–10% TRR), BF421-20 glucoside 10–18% TRR), BF421-36 glucoside (19–25% TRR) and BF421-10 (11% TRR).

In summary, for sugar beet the major degradation reactions were N oxidation of the morpholine ring, hydroxylation at the *t*-butyl moiety and subsequent conjugation reactions (glucosylations and malonylation), cleavage (detachment of the morpholine ring) or decomposition of the morpholine ring system to form hydroxypropylamine derivatives.

Barley

The metabolic fate of [^{14}C]-fenpropimorph (B-label) in barley plants maintained in a greenhouse was examined following topical application to selected leaves when plants were at the five leaf tillering stage. The application rate was equivalent to 0.9 kg ai/ha. Fenpropimorph accounted for 62% of the applied radioactivity on treated leaves at day 0, declining to 10% of applied radioactivity at day 20 after application with surface wash accounting for most of the fenpropimorph recovered (7.8%TRR). Limited translocation of radioactivity occurred to other plant parts. Fenpropimorph is a significant component of the residue in barley leaves, declining as a proportion of the total residues with increasing time after application.

Wheat

Three studies were made available on the metabolism of ^{14}C-fenpropimorph in wheat.

The metabolism of [^{14}C]-fenpropimorph in wheat grown in an open greenhouse was studied following application of the M2-label to plants at 1.3 kg ai/ha 55 days after seeding. At harvest, 84 days after treatment, TRR in grain and straw were 0.43 and 12 mg eq/kg respectively.

Methanol extracted 9% TRR in grain, 62% TRR in straw and 79–87% TRR in forage.

Extracted residues in grain were too low to characterise while residues unextracted by methanol were identified as starch 49% TRR, protein 16% TRR and polysaccharides 5% TRR.

Fenpropimorph was the major component of the residue in forage (38–47% TRR) and straw (22% TRR) with BF421-1 (7–8% TRR) and BF421-7 (5–26% TRR) the other significant components.

In a separate study with ^{14}C-fenpropimorph labelled in either the morpholine (M1-label) or phenyl (P-label) rings, wheat was treated at 0.75 kg ai/ha five weeks after sowing with harvest 56–57 days later.

Methanol extracted 52–97% TRR from forage, 56–61% TRR from straw and 12–13% TRR from grain.

TRR in methanol extracts of grain were too low to permit their characterisation. Only small amounts of ^{14}C were incorporated into polysaccharides and proteins (<10% TRR) with the majority associated with starch (31–32% TRR).

Fenpropimorph was the main component of the residue found in forage 21 days after application at 16–27% TRR, with no other single component accounting for more than 4.9% TRR.

Fenpropimorph was also the major component in straw at 20–24% TRR with BF421-2 accounting for up to 7.0% TRR. The largest individual unidentified component accounted for 7 to 12% TRR. About 12% TRR in straw was associated with lignin fractions.

In the third and most comprehensive study, two foliar applications of ^{14}C-fenpropimorph were made to wheat, each at 0.75 kg ai/ha. Fenpropimorph was labelled in the morpholine (M1-label) or phenyl (P-label) rings. Harvest was 49 days after the last application.

TRRs in hay 25 DALA were 25–48 mg eq/kg. At harvest, 49 DALA, levels of ^{14}C in grain and straw were 0.13–0.34 and 9.6–15 mg eq/kg respectively.

The extractability of ^{14}C with methanol depended on the matrix under investigation and was high for wheat hay (83–83 %TRR) and moderate for wheat straw (67–71% TRR). From the wheat grain, 15% TRR (M1-label) and 35% TRR (P-label) were extracted with methanol.

For the M1-label experiment, major identified components in grain extracts were the parent compound (1.7% TRR) and its N oxide (BF421-14, 0.6% TRR) as well as 2,6-DMM (BF421-10, 0.6% TRR). Additional components were minor amounts of the BF421-1 malonylglucoside (0.3% TRR) and the non-separated metabolites BF421-1 diglucoside and/or BF421-1 glucoside and/or BF421-20 (0.3% TRR). Sugar, predominantly fructose, accounted for 6.5% TRR.

In grain extracts (P-label), the major components were fenpropimorph (16% TRR) and its N oxide (BF421-14, 4.1% TRR) together with BF421-1 malonylglucoside (4.7% TRR), and the non-separated metabolites BF421-1 diglucoside and/or BF421-1 glucoside and/or BF421-20 (3.2% TRR).

Residues remaining in grain solids after methanol extraction, 85% TRR for M1-label and 65% TRR for the P-label, were further characterised using enzymes, acid and base, which released an additional 56% TRR from the M1-label solids, mostly as sugars, and 40% from the P-label.

In hay extracts from the M1-label experiment the major components identified were BF421-1 malonylglucoside (20 %TRR), parent compound (21 %TRR) and its N oxide (BF421-14, 14% TRR), 2,6-dimethylmorpholine (BF421-10; 6.5% TRR) and the non-separated metabolites BF421-1 diglucoside and/or BF421-1 glucoside and/or BF421 20 (7.2% TRR).

In hay (P-label) the major components in extracts were parent compound (20% TRR) and its N oxide (BF421-14, 14% TRR) and BF421-1 malonylglucoside (22% TRR). A component that represented the metabolites BF421-1 diglucoside and/or BF421-1 glucoside and/or BF421-20 accounted for 7.9% TRR.

Similar metabolic profiles to hay were obtained for straw extracts. The M1-label straw extracts contained BF421-1 malonylglucoside (16 %TRR), fenpropimorph (7.1% TRR) and its N oxide (BF421-14, 14% TRR), BF421-10 (6.4% TRR) and the non-separated metabolites BF421-1 diglucoside and/or BF421-1 glucoside and/or BF421-20 (6.7% TRR).

The major components in the P-label experiment were BF421-1 malonylglucoside (15 %TRR), the parent compound (6.9% TRR) and its N oxide (BF421-14, 12% TRR) and the non-separated metabolites BF421-1 diglucoside and/or BF421-1 glucoside and/or BF421-20 (7.8 %TRR).

The solids after methanol extraction of hay accounted for 17% TRR for the M1-label or 17% TRR for the P-label, respectively. In straw, the ^{14}C in solids after extraction were 29% TRR for the M1-label or 33% TRR for the P-label. More than 90% of the ^{14}C in the solids was released by sequential solubilisation treatments, which included aqueous ammonia, Macerozyme and cellulase,

amylases and amyloglucosidase, tyrosinase and laccase, or reflux with NaOH. The more severe treatments released additional portions of the more polar metabolites (particularly of glucoside conjugates and of BF421-10), hydroxylated metabolite BF421-1 and BF421-10 (M1-label only) and in some cases minor amounts of the parent compound and the metabolite BF421-7. Considerable amounts of the ^{14}C in solids after methanol extraction consisted of fenpropimorph or its degradation products associated with or embedded/incorporated in insoluble natural polymers (starch and cell wall components like hemicelluloses, lignin, lignin-carbohydrate complexes or pectin).

In summary, the metabolism of fenpropimorph by plants is well understood consisting of oxidative processes affecting the morpholine ring, the tertiary-butyl side chain and the methyl-propyl bridge. In addition, cleavage of the morpholine bond and glucose conjugation of a number of metabolites was also observed. A number of metabolites were not observed in laboratory animal (rat) studies. Plant specific metabolites were BF421-13 (wheat forage/straw), BF421-14 (sugar beet leaves, wheat forage/straw/grain), BF421-15 (wheat forage/straw) and BF421-36 (sugar beet leaves, wheat straw).

The possible impact of plant metabolism on the isomer ratio of fenpropimorph indicates slight enrichment of the (-)-enantiomer over the (+)-enantiomer.

Animal metabolism

Metabolism studies were made available to the meeting for lactating goats and laying hens dosed with fenpropimorph.

Lactating goats were orally dosed by intubation once daily for five consecutive days with [^{14}C]-fenpropimorph at a dose equivalent to 2336 ppm in the diet for the P-label or 1421 ppm in the diet for the M2-label.

By five hours after the last dose, the majority of the ^{14}C residues was recovered in the excreta (M2-label; urine 21% administered dose (AD), faeces 29% AD: P-label; urine 14% AD, faeces 20% AD). For tissues, ^{14}C residues were highest in kidney, (53 M2-label, 233 P-label mg eq/kg) and liver (124 M2-label, 141 P-label mg eq/kg) with muscle (6.3 M2-label, 8.9 P-label mg eq/kg) and fat (19 M2-label, 4.3 P-label mg eq/kg) containing low residues. TRR in milk reached 23 (M2-label) and 9.7 (P-label) mg equivalents/kg before the end of dosing. Overall accountability of the administered dose was poor at 55% for the M2-label and 40% for the P-label.

The whey fraction of milk from the M-label experiment contained 60 %TRR (9.8% *n*-hexane soluble; 7.5% CH_2Cl_2 soluble; 43% TRR water-soluble) with the protein fraction accounting for 33% TRR (4.7%TRR CH_3OH soluble). Radioactivity in milk from the P-label experiment was predominantly found in the whey fraction, at 76 %TRR with the remainder in the protein fraction.

Extractability of kidney, liver and muscle tissues with methanol was high at >83% TRR.

Parent fenpropimorph was not detected in any tissue or in milk. The major components of the ^{14}C in tissues and milk were BF421-2 (11–68% TRR) and BF421-1 (25–26% TRR).

In an additional study, lactating goats were orally dosed by gavage once daily for seven consecutive days with [^{14}C]-fenpropimorph at a dose equivalent to 13 ppm in the diet for the M1-label or 12 ppm in the diet for the P-label.

By 23 hours after the last dose, the majority of the ^{14}C residues were recovered in the excreta (M1-label; urine 24% AD, faeces 43% AD: P-label; urine 26% AD, faeces 50% AD). For tissues, ^{14}C residues were highest in liver (0.78 M1-label, 0.64 P-label mg eq/kg), fat (0.24 M1-label, 0.19 P-label mg eq/kg) and kidney, (0.26 M1-label, 0.15 P-label mg eq/kg) with muscle (0.06 M1-label, 0.02 P-label mg eq/kg) containing low residues.

Residues in milk appeared to reach plateau levels of 0.16 M1-label and 0.016 P-label mg eq/kg by day four of dosing with significant differences in ^{14}C levels between milk collected in the morning prior to dosing compared to evening milk, suggesting fenpropimorph residues are rapidly eliminated following dosing. The rapid elimination was confirmed by ^{14}C in plasma, which peaked at

1–6 hours after last dosing and thereafter declined with a half-life of 14–18 hours (M1-label) and 43–67 hours (P-label).

Extractability was high with > 70% TRR in kidney, liver and muscle samples extracted with methanol (71–78% M1-label, ≥ 93% P-label). For fat, methanol extracted 49% (M1-label) to 57% TRR (P-label), with iso-hexane extracting an additional 19% (P-label) to 21% (M1-label) TRR. In the case of milk, acetone/CH_3CN extracted 22% (M1-label) to 60% TRR (P-label), with methanol extracting an additional 9.7% (M1-label) to 17% (P-label) TRR.

In solvent extracts of milk, fenpropimorph (1.4–14% TRR) and the metabolites BF421-2 (2.9–27% TRR) and BF421-3 (1.1–10% TRR) were the main components identified. For the M1-label experiment, lactose accounted for up to 19% TRR with an additional 41% TRR associated with metabolites derived from 2,6-DMM. The protein precipitate accounted for 22–33% TRR (M1 and P-labels).

In liver extracts, the predominant components identified were BF421-2 (57–73% TRR) together with smaller amounts of BF421-3 (5.1–6.4% TRR), BF421-1 (1.9–10% TRR) and fenpropimorph (2.3–6.9% TRR).

The main components identified in kidney extracts were BF421-2 (25–40% TRR) and BF421-3 (21–40% TRR) and fenpropimorph (10–15% TRR). The metabolites BF421-10 (1.7% TRR) and BF421-19 (5.0% TRR) were identified exclusively in M1-label extract.

The main radioactive residue in muscle extract was BF421-2 (30–79% TRR) while components identified in fat extracts were mainly BF421-2 (29–34% TRR), BF421-2 glucuronide (14–15% TRR) and fenpropimorph (2.9–14% TRR).

The majority of ^{14}C unextracted with solvent was released on treatment of solids with pronase or acid suggesting incorporation into natural products.

Two studies on laying hens were made available to the Meeting.

In the first laying hens were orally dosed by intubation once a day for five doses with [^{14}C]-fenpropimorph at a dose equivalent to 21 ppm (M2-label) or 56 ppm (P-label) in the feed.

Excretion of fenpropimorph was fast, with 79% AD (M2-label) and 83% AD (P-label) found in the excreta by 5 hours after the last dose.

TRR for the M2-label were greatest in liver (3.9 mg eq/kg), egg yolk (3.0 mg eq/kg) and kidneys (2.4 mg eq/kg) with lower levels in the fat (1.1 mg eq/kg) and muscle (0.34 mg eq/kg). For hens dosed with the P-label, TRR were highest in liver (2.8 mg eq/kg) and kidneys (2.8 mg eq/kg), followed by fat (1.4 mg eq/kg), muscle (0.42 mg eq/kg) and eggs (0.39 mg eq/kg). Residues in the whites of eggs from both labels reached a plateau approximately 48 hours after the first dose, whereas in the yolks they continued to increase throughout the collection period, a pattern consistent with the physiology of egg formation.

Extractability with solvents and water was high at 87% for liver and kidney (80% methanol, methanol, acetone), 97% muscle (80% methanol, methanol, Soxhlet), 99% fat (methanol, ethyl acetate) and > 62% egg white and yolks (acetone).

In liver, fenpropimorph was extensively metabolised with up to 10 metabolites identified in the organosoluble extracts but no parent compound. Fenpropimorph was detected in kidney for birds dosed with the P-label. Metabolites identified were BF421-1 (plasma), BF421-2 (plasma, liver 3.9% TRR and kidney 3.5% TRR), and BF421-3 (kidney 1.9% TRR).

In a more recent study, laying hens were orally dosed once a day for ten days with [^{14}C]-fenpropimorph at a dose equivalent to 12–14 ppm in the feed (M1-label or P-label).

Radioactivity recovered from excreta together with cage wash amounted to 85% and 106% AD for the M1-label and the P-label, respectively.

The TRR in tissues were 0.097–0.63 mg eq/kg for the M1-label and 0.036–0.34 mg eq/kg for the P-label with highest residues in liver, fat, and lowest residues in muscle. In eggs, by the end of dosing the TRRs were 0.64 mg eq/kg and 0.11 mg eq/kg, for the M1- and P-label, respectively.

Extractability with methanol was generally low to moderate, at 18–56% TRR depending on label and tissue type. Subsequent extraction with iso-hexane was especially successful for fat for both labels (extracting 60–83% TRR), for the P-label muscle (66% TRR) and the M1-label egg (45% TRR). The overall extracted radioactivity using methanol + iso-hexane ranged from 46 to 101% TRR in edible matrices for the M1-label, and from 63 to 92% TRR for the P-label.

Parent fenpropimorph was a major component in eggs, fat and liver of the P-label, accounting for 18, 18 and 29% TRR respectively, whereas in the M1-label tissues fenpropimorph accounted for only 2.7% TRR in egg, 13% TRR in fat and 11% TRR in liver. In muscle, fenpropimorph represented 5.1% TRR (M1-label) and 5.5% TRR (P-label). Other compounds identified were the acid metabolite BF421-2 (eggs, muscle and liver) which was a minor component in all tissues for the M1-label (egg 1.8% TRR; muscle 0.5% TRR; liver: 1.8% TRR), but accounting for 16% TRR in eggs, 3.4% TRR in muscle and 7.5 % TRR in liver for the P-label. BF421-3 was also identified in hens in amounts similar to BF421-2, representing 13%, 2.9% and 8.1% TRR in eggs, muscle and liver of the P-label and 0.8%, 1.4% and 1.3% TRR in the respective matrices of the M1-label.

Of the M1-label specific metabolites that could be unambiguously identified, BF421-10 was found in eggs (1.5% TRR), muscle (3.4% TRR) and liver (3.3% TRR). By far the most predominant metabolites identified in the M1-label experiment were lipids in fat (79.5% TRR) and egg (45.2% TRR) with lower levels in muscle (7.6% TRR) and liver (9.8% TRR). These lipid metabolites were identified after a saponification/esterification reaction via their fatty acid methyl esters to represent triacyl glycerides primarily containing the most abundant endogenous fatty acids in hens, palmitic, oleic, and stearic acid.

The P-label specific metabolites BF421-12 and BF421-16, were identified in eggs, muscle and fat, accounting for 5.1%, 2.4% and 4.5% of the TRR. Another metabolite exclusively found in the P-label tissues was BF421-18, which was detected in the muscle in free form (4.5% TRR) and identified in all tissues as its ethyl ester after saponification/esterification, indicating an incorporation into/conjugation with endogenous lipids. Radioactive triacyl glycerides represented the major metabolites in muscle and fat, accounting for 53% and 52% TRR. They were also detected in eggs and liver, at 9.5% and 1.8% TRR, respectively.

The ^{14}C unextracted with solvent of all matrices except fat contained considerable amounts of radioactivity and were subjected to enzymatic digestion with pronase which solubilised 82 to 100% of the unextracted radioactivity. Analysis of the ^{14}C liberated by pronase treatment allowed the identification of minor amounts of parent fenpropimorph, and metabolites BF421-3, BF421-12 and BF421-16 in the egg and the identification of BF421-2 and BF421-3 in the liver of the P-label experiment. Solubilised residues of the M1-label egg, muscle and liver could not be unambiguously identified, however they were comprised of numerous compounds, presumably small polar molecules, and it is likely that a considerable portion consists of endogenous molecules.

In summary, the metabolism of fenpropimorph in lactating goats and laying hens is similar to metabolism in laboratory animals. A number of metabolites were observed in livestock but not reported in studies on laboratory animals (rats): BF421-12 (hen), BF421-18 (hen), BF421-19 (goat), BF421-21 (goat), BF421-22 (goat), BF421-26 (goat) and BF421-30 (goat). These metabolites are structurally related to the parent compound and resulted from metabolic pathways that are similar to those observed in the rat.

No information was available on the possibility for stereo-selective metabolism in livestock.

Environmental fate

The Meeting received information on soil aerobic metabolism, aqueous photolysis and aqueous hydrolysis properties of [^{14}C]-fenpropimorph. Studies were also received on the behaviour of [^{14}C]-fenpropimorph in a rotational crop situation.

The degradation of fenpropimorph in soil maintained under aerobic conditions is rapid with fenpropimorph acid (BF421-2) and BF421-10 the major degradation products formed. While parent fenpropimorph is degraded moderately fast in soils, the degradates formed can be classified as non-persistent to moderately persistent. In the laboratory studies, normalised soil DT_{50} values (20 °C pF2) for parent fenpropimorph ranged from 9.4–134 days (geometric mean 16.2 days) while for fenpropimorph acid (BF421-2) normalised DT_{50} values ranged from 3.4 to 8.9 days (geometric mean 4.6 days) and 149 days for BF421-10. In field studies an additional degradate, BF421-7 was observed for which a DT_{50} value of 82 days was estimated, consistent with laboratory studies for this metabolite for which DT_{50} values ranged from 2.5 to 209 days.

Fenpropimorph was stable to hydrolysis in aqueous solutions at pH 3 to pH 9 suggesting hydrolysis plays a negligible role in its degradation.

The soil photolysis of fenpropimorph in loamy sand soil was investigated. The half-life for degradation was estimated to be 30 days with main degradates detected BF421-13 and BF421-15. Photochemical degradation is not expected to contribute significantly to the degradation of fenpropimorph in the environment

In a confined rotational crop study with lettuce, radish and wheat, bare loamy sand soil was treated with [^{14}C]-fenpropimorph (P- and M1-labels) at the equivalent of 1.5 kg ai/ha and crops sown 30, 120 and 365 days after the soil application. Lettuce was sampled at maturity (50–56 DAA), radish was sampled at 64–76 DAA, wheat forage at 56–60 DAA and straw, chaff and grain at 95–116 DAA.

The TRRs in lettuce head were highest in the samples from the 30 days PBI (0.06–0.13 mg eq/kg) declining for subsequent plant back periods. TRRs in radish leaves (30 PBI: 0.03–0.23 mg eq/kg,) were higher than in radish roots (30 PBI: 0.02–0.04 mg eq/kg). In both matrices and both labels, the TRRs were lower for the longer PBIs. In wheat forage residues (highest 30 PBI 0.13–0.65 mg eq/kg) declined for the longer PBIs. In wheat straw and chaff, the TRRs were higher (0.36–1.2 mg eq/kg, straw) in the samples of the 30 days PBI and were 0.16–0.36 mg eq/kg for the 365 days PBI. In wheat grain TRRs at the different PBIs followed the order 120 > 30 > 365 days for the M1-label and 365 > 120 > 230 days for the P-label.

In addition to BF421-1 (free and conjugated) and BF421-10, other compounds identified were natural sugars like glucose, fructose and saccharose as well as starch.

Residues above 0.01 mg/kg were observed in the M1-label experiment at the 30-day PBI for BF421-10 (0.06 mg/kg lettuce, 0.1 mg/kg radish leaf, 0.011 mg/kg radish root, 0.42 mg/kg wheat forage, 0.58 mg/kg straw and 0.14 mg/kg chaff) and BF421-1 free and conjugated (0.016 mg/kg wheat forage, 0.031 mg/kg straw), at the 120-day PBI for BF421-10 (0.02 mg/kg lettuce, 0.03 mg/kg radish leaf, 0.04 mg/kg wheat forage, 0.13 mg/kg straw, 0.27 mg/kg chaff) and the 365-day PBI for BF421-10 (0.02 mg/kg wheat forage, 0.09 mg/kg straw and 0.02 mg/kg chaff).

In the P-label experiment fenpropimorph-related components above 0.01 mg/kg at the 30 day PBI were fenpropimorph (0.02 mg/kg lettuce, 0.05 mg/kg wheat forage) and BF421-1 free and conjugated (0.01 mg/kg lettuce, 0.06 mg/kg wheat forage, 0.28 mg/kg straw, 0.05 mg/kg chaff). No components other than natural products were above 0.01 mg/kg in the 120-day or 365-day PBI experiments.

Comparison with primary metabolism studies shows that the pathway in rotational crops is consistent with that in primary crops.

Noting that in the rotational fenpropimorph application was to bare soil and in practice a crop would be present to intercept most of the active ingredient together with the low levels detected, the Meeting concluded that, with the exception of BF421-10, fenpropimorph and related residues are unlikely to be observed in rotational crops.

Methods of analysis

The methods all involve homogenisation followed by extraction of the homogenised samples with an organic/aqueous solvent mixture, typically CH_3OH. The main differences between methods involve

clean-up conditions and instrumentation for quantification (GC-N-FID, GC-ECD, GC-NPD, GC-MS, HPLC-UV, LC-MS/MS). In plant commodities, fenpropimorph is the analyte determined while in animal commodities in addition to fenpropimorph, BF421-2 may also be determined. The LOQs for plant commodities are typically 0.01–0.05 mg/kg for fenpropimorph while for animal commodities they are 0.005 to 0.01 mg/kg for tissues and eggs and 0.001–0.002 mg/kg for milk for fenpropimorph and BF421-2.

Radiovalidation studies supported the use of CH_3OH for the extraction of residues.

Multi-residue methods are currently available for fenpropimorph in both plant and animal matrices.

Stability of pesticide residues in stored analytical samples

The Meeting received information on the stability of fenpropimorph and BF421-2 (fenpropimorph acid) in various matrices on freezer storage (-18 °C).

The periods of demonstrated stability cover the frozen storage intervals used in the residue studies on crops.

Fenpropimorph is stable in dry commodities (wheat grain) and high starch commodities (sugar beet root), high water content commodities (banana, wheat forage, sugar beet tops), high oil content commodities (sunflower seed) and wheat straw for at least 723 days.

Fenpropimorph is stable in muscle for 760 days, and at least 880 days in fat, kidney, liver, milk and cream. Fenpropimorph acid (BF421-2) is stable in liver for 760 days and muscle, fat, kidney, milk and cream for at least 880 days.

The demonstrated frozen storage stability intervals encompass the storage intervals encountered in the supervised residue trials.

Definition of the residue

The fate of fenpropimorph was investigated after foliar application to banana, sugar beet, barley and wheat plants. Fenpropimorph was degraded in all crops to a number of metabolites and their conjugates.

In edible commodities, fenpropimorph was a significant component of the radioactive residue, cereals (barley, wheat grain 2–16% TRR), root and tuber vegetables (sugar beet roots 17–34% and leaves 5–19% TRR) and tropical fruit (banana 3–60% TRR). Other significant components were BF421-36 glucoside in beet leaves (19–25% TRR), BF421-10 in beet leaves (11% TRR), BF421-20 glucoside in beet roots (11% TRR) and leaves (10–18% TRR), BF421-14 in grain (0.6–4% TRR) and beet leaves (7–10% TRR) and BF421-1 glucoside in beet leaves (10% TRR).

In livestock feeds, fenpropimorph was the major component of the residue in wheat forage (16–47% TRR). Apart from incorporation into natural products, BF421-1 and its conjugates were the most abundant components of the ^{14}C residue in wheat hay and straw (8–36% TRR) together with BF421-14 (12–14% TRR), BF421-7 (1–26% TRR) and BF421-10 (3–12% TRR).

With the exception of BF421-10, residues derived from fenpropimorph are unlikely to occur in rotational (follow) crops.

Fenpropimorph was the only compound that is a significant residue in most commodities and validated analytical methods are available for its determination.

The Meeting decided the residue definition for compliance with MRLs in plants should be fenpropimorph.

In deciding which additional compounds should be included in the residue definition for risk assessment the Meeting considered the likely occurrence of the compounds and the toxicological properties of the candidates BF421-1 (free and conjugated), BF421-7, BF421-10, BF421-14, BF421-20 conjugates and BF421-36 conjugates.

The metabolites fenpropimorph alcohol (BF 421-1 free and conjugated) and BF 421-10 are major rat metabolites and their toxicity is therefore covered by the toxicological properties of the parent compound. Testing did not reveal evidence that BF421-10 is genotoxic. For BF421-14 (fenpropimorph N-oxide) no structural alerts indicating genotoxicity were identified with the structure-activity relationship models OASIS-TIMES and VEGA.

The other plant metabolites were shown to be structurally related to the parent compound and resulted from metabolic pathways that are similar to those observed in the rat. It is considered that these metabolites are of no greater potency compared to the parent compound.

The levels of metabolites were considered in the edible commodities banana, cereal grain and young sugar beet leaves (32 DALA). Residues of BF421-1 (free and conjugated) were only present at greater than 0.01 mg/kg in sugar beet leaves. BF421-7 was only detected in grain at 49 DALA but only at levels below 0.01 mg/kg. BF421-10 and BF421-14 were detected in grain 49 DALA but also at levels below 0.01 mg/kg. BF421-20 glucoside was detected in beet roots at levels below 0.01 mg/kg. BF421-36 glucoside was not detected in commodities suitable for human consumption considered by the current Meeting.

It was noted that the typical PHIs for the approved use patterns made available to the Meeting were sometimes considerably shorter than the interval between last application and sampling in the metabolism studies, which could result in over-emphasising the relative importance of metabolites:

- Cereals (barley, rye, oats, triticale, wheat): PHI 35 days, range 28–56 days versus 49–84 days for metabolism, with the critical study samples at 49 days for grain and straw.
- Sugar beet: 35 days (range 21–46 days) versus 32 to 112 days with the critical metabolism study samples at 112 days.

Noting the above the Meeting considered only fenpropimorph and BF421-1 (free and conjugated) and BF421-10 would make significant contributions to the overall toxicological burden.

It is possible BF421-10 is not a metabolite unique to fenpropimorph as other morpholine fungicides such as aldimorph, dodemorph and tridemorph also contain the 2,6-dimethylmorpholine moiety, though their structures suggest limited potential for release of intact BF421-10 as cleavage of an amine alkyl bond would be required.

The Meeting decided the residue definition for estimation of dietary intake in plants should be the sum of fenpropimorph, BF421-1 (free and conjugated) and BF421-10 (2,6-DMM).

To facilitate estimation of exposure, a conversion factor could be used to provide a conservative estimate of the sum based solely on residues of fenpropimorph. Based on the available metabolism studies with the M-label, appropriate conversion factors (CF = [fenpropimorph+BF421-1 free and conjugated + BF421-10]/fenpropimorph) are banana 1 (metabolism sample 0 DALA), cereal grains 1.7 (44 DALA), sugar beet roots 1.3 (32 DALA) and beet leaves 3.6 (32 DALA).

For livestock dietary burden it is noted that the main residue in livestock is BF421-2 (fenpropimorph acid) and that both fenpropimorph and BF421-1 (fenpropimorph alcohol) could be transformed into BF421-2 by livestock. In considering livestock dietary burden, the sum of fenpropimorph and BF421-1(free and conjugated) residues needs to be considered. Residue trials did not measure BF421-1 and to enable a more reliable estimate of livestock dietary burden a conversion factor should also be employed (CF = [fenpropimorph+BF421-1 free and conjugated]/fenpropimorph). Based on the metabolism studies a factor of 6.15 (mean of 5.7, 6.6; 49 DALA) for straw and 1.95 (median of 1.1, 1.2, 2.7, 3.0; 21-28 DALA) for forage/hay, 1.5 (mean of 1.4, 1.6; 49 DALA) for grain, 3.6 (32 DALA) for beet tops and 1.3 (32 DALA) for beet roots should be used.

Livestock may be exposed to fenpropimorph derived residues present in feeds. The nature of fenpropimorph residues in commodities of animal origin was investigated in metabolism studies including two studies in lactating goats and two studies in laying hens. In the early studies on lactating goats and laying hens, sacrifice was 5 hours after the last dose while in the more recent studies

sacrifice was 23 hours after the last dose. The interval between last dose and sacrifice is expected to have a significant impact on the relative proportions of the metabolites detected in tissues whereas metabolite profiles for milk and eggs would be expected to be similar in the two studies.

In the more recent study on lactating goats with sacrifice 23 hours after the last dose, fenpropimorph was detected in all tissues and milk (as %TRR: milk 1.4–14%, kidney 10–15%, liver 2–7%, muscle 5% and fat 3–14%). The major components of the radioactive residues were BF421-2 free (as %TRR milk 2.9–27%, kidney 25–40%, liver 57–73%, muscle 30–79%, fat 29–34%) and conjugated (milk 0.9–3.7%, muscle 7% and fat 14–15%) and BF421-3 free and conjugated (milk 7–14% TRR, kidney 20–41% TRR, liver 6–6% TRR, muscle 6–22% TRR and fat 8–9% TRR).

The earlier study in laying hens with sacrifice at the more relevant 5 hours after the last dose did not detect fenpropimorph in tissues or eggs. The only metabolite identified was BF421-2 and then only in kidney. In the more recent study fenpropimorph was the major component identified (egg 2.7–18% TRR, liver 11–29% TRR, muscle 5% TRR, fat 13–18% TRR) with BF421-2 free and conjugated (egg 1.8–16% TRR, liver 1.8–8% TRR, muscle 0.5–3.4% TRR) and BF421-3 free and conjugated (egg 0.8–13% TRR, liver 1.3–8.1% TRR, muscle 1.4–2.9% TRR).

In livestock, fenpropimorph and BF421-2 comprised the major portion of the residue in tissues, milk and eggs and validated analytical methods are available for their determination.

The Meeting decided the residue definition for compliance with MRLs in livestock commodities should be the sum of fenpropimorph and BF421-2.

In deciding which additional compounds to fenpropimorph should be included in the residue definition for risk assessment the Meeting considered the likely occurrence of the compounds and the toxicological properties of the candidates BF421-2 (free and conjugated) and BF421-3 (free and conjugated).

The metabolites BF421-2 (free and conjugated) and BF421-3 (free and conjugated) are major rat metabolites and their toxicity is therefore covered by the toxicological properties of the parent compound.

As the contribution of the additional metabolites BF421-2 glucuronide and BF421-3 and its glucuronide to the overall consumer exposure would be small, the Meeting decided the definition for estimation of dietary exposure should be the sum of fenpropimorph and BF421-2.

In summary, based on the above the Meeting decided the residue definitions for compliance with MRLs and estimation of dietary intake should be as follows:

Definition of the residue for compliance with MRL for plant commodities: fenpropimorph

Definition of the residue estimation of dietary intake for plant commodities:

sum of fenpropimorph, fenpropimorph alcohol (free and conjugated) and BF421-10 (2,6-DMM), expressed as fenpropimorph.

Definition of the residue for compliance with MRL and estimation of dietary intake for animal commodities: sum of fenpropimorph and fenpropimorph acid (BF421-2) expressed as fenpropimorph

Residues (sum of fenpropimorph and BF421-2) in fat were more than 5× greater than muscle in the lactating goat and laying hen metabolism studies. However, in the livestock transfer study with lactating cows, residues in fat are only slightly greater than muscle and residues in cream are only about 2× residues in skim milk. On the weight of evidence, the Meeting decided residues measured as the sum of fenpropimorph and BF421-2 are not fat soluble.

The residue is not fat soluble.

Results of supervised residue trials on crops

Supervised residue trial data for were available for fenpropimorph on bananas, sugar beet, barley, oats, rye and wheat.

Banana

The Meeting received supervised residue trial data for fenpropimorph on banana from Brazil, Colombia, Costa Rica, Ecuador, Guatemala, Honduras, Martinique and Mexico. In Columbia critical GAP is applications at up to 0.6 kg ai/ha with a PHI 0 days. In trials approximating critical GAP in Columbia (0.6±25% kg ai/ha) residues in unbagged bananas were: (n=18): < 0.05, < 0.05, < 0.05, 0.07, 0.1, 0.12, 0.13, 0.16, 0.26, 0.32, 0.36, 0.43, 0.65, 0.7, 0.7, 0.8, 1.2, 1.4 mg/kg.

The Meeting estimated a maximum residue level of 2 mg/kg for bananas, confirming its previous recommendation.

Residues in the edible portion (pulp) were (n=11): < 0.05, < 0.05, < 0.05, < 0.05, 0.06, 0.08, 0.14, 0.18, 0.28, 0.30, 0.43 mg/kg. The Meeting recommended an STMR and HR of 0.08 and 0.43 mg/kg respectively for banana (pulp).

The Meeting also noted that the STMR and HR are conservative as residues in bagged bananas, a common commercial practice, were lower than for unbagged bananas with residues in pulp for bagged bananas that ranged from < 0.05 to 0.2 mg/kg.

Sugar beet

In Poland critical GAP is a single application at 0.25 kg ai/ha at growth stage BBCH 39–49 with a 35 day PHI. In trials conducted in Europe on sugar beet the application rate (0.75 kg ai/ha) was higher than the critical GAP of Poland (0.25 kg ai/ha) and the Meeting agreed to utilise the proportionality approach (scaling factor 0.75/0.25=0.33) to estimate residues matching cGAP. Unscaled residues for sugar beet were (n=8) < 0.01 (7), 0.06 mg/kg. Residues below LOQ were not scaled. After scaling the following residues were obtained (n=8), < 0.01 (7) and 0.02 mg/kg.

The Meeting recommended a maximum residue level of 0.03 mg/kg to replace its previous recommendation of 0.05 * mg/kg and an STMR for dietary intake estimation and median residue for livestock feeds of 0.013 (1.3×0.01) mg/kg for sugar beet.

Barley

Supervised residue trial data for fenpropimorph on barley were made available. The critical GAP in Belgium is up to two applications at 0.75 kg ai/ha with a PHI of 28 days.

In trials conducted in Europe and Brazil approximating critical GAP in Belgium (0.75±25% kg ai/ha), residues in barley were (n=15): 0.01, 0.02, 0.02, 0.02, < 0.05, < 0.05, < 0.05, < 0.05, < 0.05, 0.07, 0.07, 0.07, 0.09, 0.11 and 0.11 mg/kg.

The Meeting recommended a maximum residue level of 0.2 mg/kg, an STMR of 0.085 (1.7×0.05) mg/kg for dietary intake estimation and a median residue of 0.075 (1.5×0.05) mg/kg for livestock dietary burden estimation for barley. Use patterns exist for oats and the Meeting decided to extrapolate the values to oats. The recommendations for barley and oats replace the previous recommendations of 0.5 mg/kg for these commodities.

Wheat

Supervised residue trial data for fenpropimorph on wheat were available. Critical GAP in Belgium is two applications at 0.75 kg ai/ha with a PHI of 28 days.

In trials conducted in Europe approximating critical GAP in Belgium residues in wheat grain were (n=7): < 0.01, < 0.01, < 0.01, < 0.01, 0.01, 0.02, and 0.04 mg/kg.

The Meeting recommended a maximum residue level of 0.07 mg/kg, an STMR of 0.017 (1.7×0.01) mg/kg for dietary intake estimation and a median residue of 0.015 (1.5×0.01) mg/kg for livestock dietary burden estimation for wheat. Use patterns exist for rye and triticale and the Meeting decided to extrapolate the values to rye and triticale.

The recommendations for rye, triticale and wheat replace the previous recommendations for these commodities.

Animal feedstuffs

Sugar beet tops

In Poland critical GAP is a single application at 0.25 kg ai/ha at growth stage BBCH 39–49 with a 35 day PHI. In trials conducted in Europe on sugar beet the application rate (0.75 kg ai/ha) was higher than the critical GAP of Poland (0.25 kg ai/ha) and the Meeting agreed to utilise the proportionality approach (scaling factor 0.31–0.35) to estimate residues matching cGAP. Unscaled residues for sugar beet tops were (n=8) 0.11, 0.15, 0.17, 0.2, 0.21, 0.22, 0.33 and 0.44 mg/kg. After scaling the following residues were obtained: 0.04, 0.05, 0.06, 0.06, 0.07, 0.07, 0.11 and 0.14 mg/kg. Sugar beet tops contain approximately 23% DM.

The Meeting noted that sugar beet tops are not a traded commodity and decided to withdraw its previous recommendation for fodder beet leaves and tops of 1 mg/kg. The Meeting also estimated a median residue of 0.367 (1.3×0.065/0.23) mg/kg and a highest residue of 0.848 (1.3×0.15/0.23) mg/kg (all on dry matter basis) for livestock dietary burden estimation for sugar beet leaves and tops.

Cereal straw

Supervised residue trial data for fenpropimorph on barley were made available. The critical GAP in Belgium is up to two applications at 0.75 kg ai/ha with a PHI of 28 days. Residues in barley straw from trials complying with critical GAP were (n=16): < 0.05, < 0.05, 0.03, 0.04, 0.04, 0.07, 0.08, 0.08, 0.1, 0.13, 0.14, 0.14, 0.15, 0.16, 0.17 and 0.39 mg/kg.

For wheat, the critical GAP in Belgium is up to two applications at 0.75 kg ai/ha with a PHI of 28 days. Residues in wheat straw in trials approximating cGAP were (n=7): 0.07, 0.07, 0.11, 0.12, 0.14, 0.21 and 0.34 mg/kg.

The Meeting noted that residues in barley and wheat straw are similar, confirmed by a Mann-Whitney U test, and decided to combine the data sets for mutual support. The combined data is: < 0.05, < 0.05, 0.03, 0.04, 0.04, 0.07, 0.07, 0.07, 0.08, 0.08, 0.1, 0.11, 0.12, 0.13, 0.14, 0.14, 0.14, 0.15, 0.16, 0.17, 0.21, 0.34 and 0.39 mg/kg.

The Meeting recommended a maximum residue level of 0.5 mg/kg and median 0.68 (6.15×0.11) mg/kg and highest 2.40 (6.15×0.39) mg/kg residues for use in estimation of livestock dietary burden for barley and wheat straw and fodder, dry. The Meeting agreed these values should be extrapolated to oats, rye and triticale straw and fodder, dry and replace the previous recommendations.

Fate of residues during processing

The Meeting received information on the nature of the residue of fenpropimorph under simulated processing conditions (pasteurization 20 minutes at 90 °C, pH 4, baking/brewing/boiling 60 minutes at 100 °C, pH 5, sterilization 20 minutes at 120 °C, pH 6) showed fenpropimorph, if present, is hydrolytically stable under processing conditions representative of pasteurisation, baking/boiling/brewing and under sterilisation conditions.

A number of processing studies on sugar beet, barley, oats and wheat were reviewed by the Meeting. A summary of relevant fenpropimorph processing factors is provided below.

	Processed Fraction	Processing Factor (PF)[A]	Best estimate PF	RAC STMR or median	STMR×PF	CF	STMR×PF×CF = STMR-P
Sugar beet	Molasses	< 0.04 < 0.06	0.05	0.01	0.0005	1.3	0.00065
	Refined sugar	< 0.04 < 0.06	0.05		0.0005		0.00065
	Dried pulp	2.9 3.9	3.4		0.034		0.0442
	Ensiled pulp	0.8 1	0.9		0.009		0.0117
Wheat	Bran	0.19 2.9 6.5	2.9	0.01	0.029	1.7	0.0493
	Flour	0.28 0.35 < 1	0.35		0.0035		0.00595
	Wholemeal flour	1.3 1.4 1.5	1.4		0.014		0.0238

	Processed Fraction	Processing Factor (PF)[A]	Best estimate PF	RAC STMR or median	STMR×PF	CF	STMR×PF×CF = STMR-P
	Wholemeal bread	1.1 1.4 3.2	1.4		0.014		0.0238
	Germ	2.4 4.2	3.3		0.033		0.0561
Barley	Brewing malt	0.7 0.8 1.2 1.4	1	0.02	0.02	1.7	0.034
	Beer	< 0.004 < 0.004 < 0.4 < 0.5	0.004		0.00008		0.000136
	Pot barley	0.6 0.8 1.0 1.6	0.9		0.018		0.0306
	Flour	2.5 2.5	2.5		0.05		0.085
Oats	Husks/dust	1 1.4 1.6 1.9	1.6	0.02	0.032	1.5	0.0544
	Oat flakes	0.5 0.8 1 1	0.8		0.016	1.7	0.0272

[A] PF = residues fenpropimorph in processed commodity divided by fenpropimorph in RAC

Residues of fenpropimorph concentrated in sugar beet pulp (dry), wheat bran, wholemeal flour, wholemeal bread, wheat germ and barley flour

The Meeting recommended the following maximum residue levels for processed commodities for which there are codes in the commodity classification: Sugar beet pulp (dry) 0.1 mg/kg (0.03×3.4=0.1 mg/kg), wheat bran (unprocessed) 0.2 mg/kg (0.07×2.9=0.2 mg/kg), wheat germ 0.3 mg/kg (0.07×3.3=0.23 mg/kg) and wheat wholemeal 0.1 mg/kg (0.07×1.4=0.098 mg/kg).

Residues in animal commodities

Farm animal feeding studies

The Meeting received information on the residue levels in tissues and milk of dairy cows dosed with fenpropimorph at the equivalent of 5, 16 and 52 ppm in the feed for 28 consecutive days.

Mean residues (max in brackets) of BF421-2 in milk were 0.012, muscle 0.03 (0.04), liver 0.75 (0.94), kidney 0.09 (0.11), fat 0.02 (0.02) mg/kg for the 5 ppm dose group and in milk were 0.065, muscle 0.19 (0.31), liver 5.6 (7.8), kidney 0.73 (0.92), fat 0.15 (0.22) mg/kg for the 52 ppm dose group.

An additional study was made available to the Meeting where dairy cows dosed with fenpropimorph at the equivalent of 2, 6 and 20 ppm in the feed for 28 consecutive days. Residues of fenpropimorph and BF421-2 in milk were 0.007 mg/kg, muscle 0.02 (0.02), liver 0.37 (0.46), kidney 0.08 (0.08), fat 0.03 (0.03) mg/kg for the 2 ppm dose group and in milk 0.046 mg/kg, muscle 0.14 (16), liver 2.9 (3.5), kidney 0.47 (54), fat 0.18 (0.22) mg/kg for the 20 ppm dose group.

A laying hens feeding study was not available.

Estimation of livestock dietary burdens

Dietary burden calculations for beef cattle and dairy cattle and poultry are provided below. The dietary burdens were estimated using the OECD diets listed in Appendix IX of the 2016 edition of the FAO Manual.

Potential cattle feed items include: cereal grain and straw and sugar beet tops.

Summary of livestock dietary burden (ppm fenpropimorph equivalents of dry matter diet)

	US-Canada		EU		Australia		Japan	
	Max	mean	Max	Mean	max	Mean	Max	Mean
Beef cattle	0.47	0.18	1.0	0.35	2.7 [A]	0.77 [C]	0.07	0.07
Dairy cattle	0.86	0.28	1.1	0.38	2.7 [B]	0.76 [D]	0.20	0.10
Broilers	0.08	0.08	0.07	0.07	0.03	0.03	0.01	0.01
Layers	0.08	0.08	0.25 [E]	0.13 [F]	0.03	0.03	0.01	0.01

[A] Highest maximum beef or dairy cattle dietary burden suitable for MRL estimates for mammalian meat

[B] Highest maximum dairy cattle dietary burden suitable for MRL estimates for mammalian milk

[C] Highest mean beef or dairy cattle dietary burden suitable for STMR estimates for mammalian meat.

[D] Highest mean dairy cattle dietary burden suitable for STMR estimates for milk.

[E] Highest maximum poultry dietary burden suitable for MRL estimates for poultry meat and eggs

[F] Highest mean poultry dietary burden suitable for STMR estimates for poultry meat and eggs

Animal commodity maximum residue levels

The calculations used to estimate highest total residues for use in estimating maximum residue levels, STMR and HR values are shown below.

	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg) in			
				Muscle	Liver	Kidney	Fat
MRL beef or dairy cattle							
Feeding study [a]	6.0	0.013	6.0	0.06	0.78	0.20	0.07
	2.0	0.007	2.0	0.02	0.46	0.08	0.03
Dietary burden and high residue	2.7	0.0077	2.7	0.027	0.516	0.101	0.037
STMR beef or dairy cattle							
Feeding study [b]	2.0	0.007	2.0	0.02	0.37	0.08	0.03
Dietary burden and median residue estimate	0.76	0.0027	0.77	0.0077	0.142	0.031	0.012

[a] highest residues for tissues and mean residues for milk

[b] mean residues for tissues and mean residues for milk

The Meeting estimated the following maximum residue levels: milk 0.01 mg/kg; meat (mammalian except marine mammals) 0.04 mg/kg, mammalian fat (except milk fat) 0.05 mg/kg and edible offal 0.7 mg/kg. The Meeting estimated the following HRs: mammalian meat 0.027 mg/kg; mammalian fat 0.037 mg/kg; liver 0.516 mg/kg, kidney 0.101 mg/kg and milk 0.0077 mg/kg and STMRs: mammalian meat 0.0077 mg/kg; mammalian fat 0.012 mg/kg; liver 0.142 mg/kg, kidney 0.031 mg/kg and milk 0.0027 mg/kg.

The Meeting agreed to withdraw its previous recommendation for Kidney of cattle, goats, pigs and sheep of 0.05 mg/kg and for Liver of cattle, goats, pigs and sheep of 0.3 mg/kg.

Although a laying hen feeding study was not available, in a metabolism study where hens were dosed at the equivalent of 12–14 ppm in the diet for ten days, residues of fenpropimorph and BF421-2 were 0.03–0.04 mg/kg in eggs, 0.003–0.005 mg/kg in muscle, 0.06 mg/kg in fat and 0.08–0.09 mg/kg in liver.

At the maximum dietary burden for poultry (0.25 ppm), no residues above typical LOQs for analytical methods are expected in eggs and tissues. The Meeting estimated the following maximum residue levels for poultry commodities: poultry meat 0.005* mg/kg; poultry edible offal 0.005* mg/kg, poultry fat 0.005* mg/kg and eggs 0.005* mg/kg to replace its previous recommendations for these commodities. The Meeting estimated the following STMR and HR values: poultry meat 0 mg/kg; poultry fat 0 mg/kg; poultry edible offal 0 mg/kg and eggs 0 mg/kg.

RECOMMENDATIONS

On the basis of the data obtained from supervised residue trials the Meeting concluded that the residue levels listed in Annex 1 are suitable for establishing maximum residue limits and for IEDI and IESTI assessment.

Definition of the residue (for compliance with MRLs) for plant commodities*: fenpropimorph*

Definition of the residue (for estimation of dietary intake) for plant commodities*: sum of fenpropimorph, 2-(4-{(2RS)-3-[(2R,6S)-2,6- dimethylmorpholin-4-yl]-2- methylpropyl}phenyl)-2-methylpropan-1-ol (free and conjugated) (BF421-1) and (2R,6S)-2,6-dimethylmorpholine (BF421-10) expressed as fenpropimorph.*

Definition of the residue (for compliance with MRLs and estimation of dietary intake) for animal commodities*: sum of fenpropimorph and 2-(4-{(2RS)-3-[(2R,6S)-2,6- dimethylmorpholin-4-yl]-2- methylpropyl}phenyl)-2- methylpropanoic acid (BF421-2) expressed as fenpropimorph*

The residue is not fat soluble.

DIETARY RISK ASSESSMENT

Long-term exposure

The 2016 JMPR established an Acceptable Daily Intake (ADI) of 0–0.004 mg/kg bw for fenpropimorph.

The evaluation of fenpropimorph resulted in recommendations for MRLs and STMR values for raw and processed commodities. Where data on consumption were available for the listed food commodities, dietary intakes were calculated for the 17 GEMS/Food Consumption Cluster Diets. The results are shown in Annex 3.

The IEDIs in the seventeen Cluster Diets, based on the estimated STMRs were 1–10% of the maximum ADI (0.004 mg/kg bw). The Meeting concluded that the long-term dietary exposure to residues of fenpropimorph from uses that have been considered by the JMPR is unlikely to present a public health concern.

Short-term exposure

The 2016 JMPR established an Acute Reference Dose (ARfD) of 0.1 mg/kg for women of child-bearing age and 0.4 mg/kg bw for the general population for fenpropimorph. The IESTI of fenpropimorph for the commodities for which STMR, HR and maximum residue levels were estimated by the current Meeting. The results are shown in Annex 4. The IESTI represented 0–5% of the ARfD for women of child-bearing age and 0–9% for the general population.

The Meeting concluded that the short-term dietary exposure to residues of fenpropimorph resulting from uses that have been considered by the JMPR is unlikely to present a public health concern.